Palladium-catalysed hydroalkoxycarbonylation of styrene in [BMIM][BF$_4$] and [BMIM][PF$_6$] ionic liquids

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Abstract

The hydroalkoxycarbonylation of styrene was carried out by using various alcohols (ethanol, *n*- and *i*-propyl alcohol, benzyl alcohol, *n*-octyl alcohol) in imidazolium-based ionic liquids. In addition to the formation of the expected 2-phenyl- and 3-phenyl-propionates, the oligomerization of the substrate depending on the reaction conditions was also observed in [BMIM][PF$_6$] and in [BMIM][BF$_4$] (to a small extent) ionic liquids. Moderate to high regioselectivities towards branched esters have been obtained in [BMIM][BF$_4$]. The highest regioselectivities towards branched ester have been observed with 'preformed' PdCl$_2$(PPh$_3$)$_2$ catalyst. The addition of diphosphines favoured the formation of the linear isomer. The application of [BMIM][PF$_6$] ionic liquid results mainly in the formation of the linear esters. The regioselectivity is strongly dependent also on the alcohol: for example, while the application of ethanol resulted in branched regioselectivities up to 50 and 81% in [BMIM][PF$_6$] and [BMIM][BF$_4$], respectively, 100% linear and 83% branched selectivities were obtained in the presence of *n*-octyl alcohol as a nucleophile.
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1. Introduction

The synthesis of carboxylic esters from easily available starting materials is one of the basic reactions in synthetic chemistry. The use of carbon monoxide as a 'carboxyl-source' in rhodium- or palladium-catalysed hydroalkoxy-carbonylation reaction is a widely known methodology for the synthesis of esters [1,2]. It has been proved with model compounds (styrene was mainly used) that the regioselectivity can be tuned by the catalyst and sensitive to the reaction parameters [3,4]. The related hydroxycarbonylation reaction shows similar sensitivity to the ligand, i.e. the formation of 2- and 3-phenyl-propionic acid is favoured in the presence of mono- and bi-dentate phosphines, respectively [5].

The olefinic functionalities in various skeletons (steroids, terpenes) can be converted to the corresponding esters of practical importance by palladium-catalysed hydroalkoxy-carbonylation [6–11]. The intramolecular version of this reaction, i.e. the carbonylation of unsaturated alcohols provides lactons in high yields [12–14].

The search for more efficient homogeneous catalytic systems raised the application of various novel solvents. In addition to the conventional organic solvents aqueous-organic, fluorous-organic systems can also be used providing facile phase separation and therefore, the re-circulation of the homogeneous catalyst [15,16]. Among the recently used alternative solvents ionic liquids play an important role due to their environmentally benign properties like extremely low vapour pressure, chemical and thermal stability, high ionic conductivity and good solvent properties towards both ionic and covalent compounds [17–21]. They have already been used in several homogeneous catalytic reactions (among them

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hydrogenation [22], oligomerization [23–25] and coupling reactions [26,27]). However, less carbonylation reactions are known in ionic liquids. Examples for hydroformylation reactions in ionic liquid have already been described in the presence of cobalt, rhodium and platinum catalysts [28–31]. To the best of our knowledge, there is a single example for the palladium-catalysed hydroalkoxycarbonylation of olefins in ionic liquid [32].

In this paper, the palladium-catalysed alkoxycarbonylation of styrene will be described. Imidazolium-based ionic liquids ([BMIM][BF₄] and ([BMIM][PF₆]) are used as solvents and various alcohols as nucleophiles.

2. Experimental

2.1. Reagents

The phosphine ligands (triphenylphosphine, dppe (1,2-bis(diphenylphosphino)ethane), dppp (1,3-bis(diphenylphosphino)propane), dppb (1,4-bis(diphenylphosphino) butane) (Aldrich)) were used without further purification. The Karl Fischer titrant (Hydranal®) was purchased from Aldrich. The methanol used for Karl Fischer titrations was a Riedel-de-Haën product. Toluene and the alcohol reactants were dried according to standard procedures.

Ionic liquids were purchased from Aldrich or prepared according to a published procedure [33]. The preparation resulted in the same quality to the purchased ones. The ionic liquids were stored under argon. Their water content was determined by Karl Fischer method and was accepted as applicable to catalytic measurements if the water content was reduced to 200 ppm. During drying and purification of [BMIM][PF₆], 10 ml of ionic liquid was dissolved in 20 ml of acetonitrile and 1 g active charcoal was added. The charcoal was filtered off and the acetonitrile was distilled off under argon. The ionic liquid was kept under high vacuum at 60 °C for 4 h and put under argon.

Styrene was freshly distilled before use. PdCl₂(PPh₃)₂ was prepared on the basis of a described method [34].

2.2. Hydroalkoxycarbonylation reaction

In a typical reaction 7.0 mg (0.01 mmol) PdCl₂(PPh₃)₂ (and in case of the in situ systems 0.01 mmol dppe or dppp or dppb) was dissolved in 0.5 ml ionic liquid under argon in a glass-tube situated in a 100 ml autoclave. Styrene (57 μl (0.5 mmol)) and 2 mmol alcohol were added. The atmosphere was changed to carbon monoxide, pressurised to 100 bar and the reaction mixture was kept at 100 °C for 24 h. After the given reaction time, the organic products were extracted by 1.0 ml of toluene at 60 °C under vigorous stirring. The mixture was cooled, the toluene phase was separated and analysed with a Hewlett Packard 5830A gas chromatograph fitted with a capillary column coated with OV-1.

3. Results

3.1. Hydroalkoxycarbonylation experiments in the presence of PdCl₂(PPh₃)₂ (+diphosphine) catalysts in [BMIM][BF₄] ionic liquid

Styrene (**1**) as a model substrate was reacted with carbon monoxide and the corresponding alcohol in the presence of either a 'preformed' palladium catalyst (Pd(PPh₃)₂Cl₂) or the in situ palladium catalyst obtained from Pd(PPh₃)₂Cl₂ and a bi-dentate phosphine ligand (dppe, dppp or dppb). Imidazolium-based ionic liquid ([BMIM][BF₄]) has been used as a solvent at 100 °C and under 100 bar carbon monoxide pressure. Although the small amounts of reactants (styrene, alcohols) are not completely miscible with ionic liquids at room temperature, at 100 °C the system is completely homogeneous. The low solubility of aromatics in ionic liquids at room temperature has been utilised for the extraction of the organic products (see Section 2).

$$RhCH{=}CH_2 \xrightarrow{CO/ROH} PhCH(COOR)CH_3 + PhCH_2CH_2COOR,$$
$$\underset{\mathbf{1}}{} \qquad \underset{\mathbf{2a\text{–}f}}{} \qquad \underset{\mathbf{3a\text{–}f}}{}$$

R = Et(**a**), nPr(**b**), iPr(**c**), tBu(**d**), Bz(**e**), nOct(**f**)

The hydroalkoxycarbonylation of styrene (**1**) resulted in the formation of the branched (2-phenylpropionic acid esters, **2a–f**) and the linear (3-phenylpropionic acid esters, **3a–f**) regioisomers.

As a general observation it has to be noted that in all cases the oligomerization (polymerization) of styrene took also place to some extent resulting in the 'loss' of part of the substrate. Furthermore, the activity of the tested palladium catalysts falls behind that of some palladium–phosphine systems in conventional solvents [4] (see also runs 5 and 6, Table 1).

As for the alcohol reactant, the ester formation is strongly dependent on the structure of the alcohol. No reaction with *tert*-butyl alcohol was observed either in the presence or absence of diphosphines (run 11).

Moderate to high regioselectivities towards branched esters have been observed depending on the phosphine added. The regioselectivity of ethoxycarbonylation was varied by the diphosphine. For example, while 81% branched selectivity was obtained in the absence of a chelating ligand, it was decreased to 17% by using the dppp containing catalytic system (runs 1 and 3).

The application of n-propyl and isopropyl alcohol by using the preformed Pd(PPh₃)₂Cl₂ catalyst resulted in 93 and 68% branched selectivity, respectively, that was decreased to 69 and 65% in the presence of dppe (runs 7 and 9, as well as 8 and 10). Similarly, the application of the n-octylalcohol resulted in the favoured formation of the branched ester **2f** with 83 and 77% regioselectivity in the presence of PdCl₂(PPh₃)₂ and that of the in situ catalyst, respectively (runs 15 and 16).

Extremely high regioselectivities have been obtained with benzyl alcohol. Regardless on the structure of the chelat-

Table 1
Hydroalkoxycarbonylation of styrene (**1**) in the presence of PdCl$_2$(PPh$_3$)$_2$ (+ligand) catalysts in [BMIM][BF$_4$] ionic liquid

Entry	Ligand added	Alcohol	Conversion[a] (%)	Branched (**2**) (%)	Linear (**3**) (%)	R_{br}[b]
1	–	EtOH	59	48	11	81
2	dppe	EtOH	5	3	2	60
3	dppp	EtOH	3	0.5	2.5	17
4	dppb	EtOH	4	2	2	50
5[c]	–	EtOH	54	52	2	96
6[c]	dppb	EtOH	35	2	33	6
7	–	*n*PrOH	59	55	4	93
8	dppe	*n*PrOH	29	20	9	69
9	–	*i*PrOH	60	41	19	68
10	dppe	*i*PrOH	26	17	9	65
11	–	*t*BuOH	0	0	0	n.d.
12	–	BzOH	93	93	0	100
13	dppe	BzOH	11	11	0	100
14	dppb	BzOH	8	8	0	100
15	–	*n*OctOH	100	83	17	83
16	dppb	*n*OctOH	100	77	23	77

Reaction conditions: Pd/styrene = 1/50; reaction temperature: 100 °C; p(CO) = 100 bar; reaction time: 24 h. The amount of styrene converted to side products (oligomers, polymers) is in the range of 2–5% and not indicated in the conversion column (calculated by GC using dodecane internal standard).

[a] Conversion of **1** to **2** and **3** are indicated in this column only (calculated by GC using dodecane internal standard).

[b] Regioselectivity towards branched ester regioisomer [mole of **2**/(mole of **2** + mole of **3**) × 100].

[c] Solvent: toluene.

ing phosphine used, practically regiospecific reaction was obtained, i.e. the branched ester regioisomer **2e** was formed exclusively (run 12–14).

3.2. Hydroalkoxycarbonylation experiments in the presence of PdCl$_2$(PPh$_3$)$_2$ (+diphosphine) catalysts in [BMIM][PF$_6$] ionic liquid

Hydroalkoxycarbonylation as a test reaction has been carried out also in [BMIM][PF$_6$] ionic liquid under the same reaction conditions as above (100 °C, 100 bar CO). As it has been observed previously, the regioselectivity of the hydroalkoxycarbonylation reaction was influenced both by the alcohol and the ligand (monodentate phosphines and diphosphines of different chain length).

The formation of the linear ester was favoured by using all of the alcohols except for *n*-propanol. In this exceptional case the regioselectivities towards branched ester **2b** were varied between 49 and 64% (Table 2, runs 6–8). In the presence of *n*-octyl alcohol the linear ester was formed exclusively regardless on the catalyst used (runs 16–19). The hydroalkoxycarbonylation with isopropanol nucleophile resulted in the prevailing formation of the linear ester and the regioselectivities towards branched ester **2c** were varied between 12 and 33% (runs 9–11). As in [BMIM][BF$_4$] ionic liquid, no ester formation was observed with *t*-butanol (run 12).

Table 2
Hydroalkoxycarbonylation of styrene (1) in the presence of PdCl$_2$(PPh$_3$)$_2$ (+ligand) catalysts in [BMIM][PF$_6$] ionic liquid

Entry	Ligand added	Alcohol	Conversion[a] (%)	Branched (**2**) (%)	Linear (**3**) (%)	R_{br}[b]
1	–	EtOH	32	13	19	41
2	dppe	EtOH	38	8	30	21
3	dppp	EtOH	4	2	2	50
4	dppb	EtOH	100	9	91	9
5[c]	dppb	EtOH	12	2	10	17
6	–	*n*PrOH	80	51	29	64
7	dppe	*n*PrOH	100	49	51	49
8	dppb	*n*PrOH	88	52	36	59
9	–	*i*PrOH	100	33	67	33
10	dppe	*i*PrOH	37	12	25	32
11	dppb	*i*PrOH	42	5	37	12
12	–	*t*BuOH	0[d]	0	0	n.d.
13	–	BzOH	22	10	12	45
14	dppe	BzOH	32	13	19	41
15	dppb	BzOH	29	15	14	52
16	–	*n*OctOH	12	0	12	0
17	dppe	*n*OctOH	14	0	14	0
18	dppp	*n*OctOH	16	0	16	0
19	dppb	*n*OctOH	81	0	81	0

Reaction conditions: Pd/styrene = 1/50; reaction temperature: 100 °C; p(CO) = 100 bar; reaction time: 24 h.

[a] Conversion of **1** to **2** and **3** are indicated in this column only (calculated by GC using dodecane internal standard).

[b] Regioselectivity towards branched ester regioisomer [mole of **2**/(mole of **2** + mole of **3**) × 100].

[c] Reaction temperature, 80 °C.

[d] ca. 30% of styrene dimers (mixture of isomers) were formed; (in the other cases the amount of the dimers are in the range of 2–5%).

As for the diphosphines used, its application resulted in the slight shift towards linear esters. The preferred formation of the branched and linear ester regioisomers in the presence of mono- and bi-dentate phosphines, respectively, is generally observed also in conventional organic solvents [35,36].

Although the main goal of this study was not to optimise a methodology for efficient reuse of the ionic liquid phase, some attempts have been made in order to recycle the ionic liquid containing the catalytically active species. The ester regioisomers, the substrate and the oligomeric byproducts can be extracted with toluene from the [BMIM][PF$_6$] phase, unfortunately, the leaching of the catalyst can also be observed. The activity of the 'recycled' catalyst decreased by 5–10% in the first three runs. In the following runs the decrease is even more drastic. (It is worth noting that some leaching and consequently, some decrease in catalytic activity upon recycling can be observed even in case of sulphonated ligands like TPPTS (tris(3-sulfanatophenyl)phosphine) [37].)

4. Discussion

Three striking features of the hydroalkoxycarbonylation of styrene in ionic liquids can be mentioned: (i) the enhanced oligomerization/polymerization reaction, (ii) the strong dependence of the regioselectivity on the ionic liquid, i.e. the

preferred formation of branched and linear esters in tetrafluoroborate and hexafluorophosphate ionic liquids, respectively, and (iii) the dependence of the regioselectivity on the alcohol.

Although hydroalkoxycarbonylation is usually accompanied by side reactions (oligomerization, polymerization) even in conventional organic solvents, the amount of the side products are much smaller. In our case, the reaction has been carried out in ionic liquids of low water content (dried before use). However, especially with hexafluorophosphate ionic liquid, the formation of oligomeric side products in various amounts could not be avoided even in ionic liquid stored under argon and used under strict conditions. They are formed as major products in case of *t*BuOH, which did not show any reactivity in hydroalkoxycarbonylation.

While dimerization of styrene is almost negligible in [BMIM][BF$_4$], the mixture of styrene dimers might be formed up to 30% in [BMIM][PF$_6$]. As it has been shown previously by ^{31}P NMR investigations, the PF$_6$$^-$ counterion cannot be considered as innocent species in transition metal catalysed reactions and a special care has to be sentenced to it [38]. Even the smallest amount of water resulted in the formation of HF and equilibrating phosphorous species showing two characteristic triplets in ^{31}P NMR. They can be assigned to 'PF$_2$' containing species [38]. The acidification of the system might be responsible for olefin polymerization to large extent. It is worth noting that the partial hydrolysis of hexafluorophoshate ion takes place even in the absence of any platinum or palladium complexes, but their presence accelerates the formation of solvent degradation products.

Attempts have been made to reduce these undesired reactions. The reduction of the temperature to 80 °C resulted in a drastic drop of the catalytic activity. (Conversion of nearly 100% dropped to 12% (Table 2, runs 4 and 5). It is worth noting that the increase of the viscosity of the ionic liquid by decreasing temperature, and as a consequence of that, the gas diffusion control might be also responsible for the low activity. The addition of further two equivalents of PPh$_3$ resulted in a slight decrease in the catalytic activity but the side products are in the same range.

The preferred formation of the linear ester regioisomer in the presence of palladium–diphosphine systems is known for a long time [35,36]. In ionic liquid the in situ formation of Pd(PP)Cl$_2$ (PP = dppe, dppp, dppb) type complexes takes place, by the substitution of triphenylphosphine by chelating diphosphines, which is responsible for the decrease of the branched selectivity, i.e. the increased formation of 3-phenyl-propionates.

On the basis of previous findings it has been suspected that the dominant activity of catalytic intermediates containing monodentate ligands could be a possible explanation for the rather high-branched selectivity in [BMIM][BF$_4$]. In fact, ^{31}P NMR experiments carried out in [BMIM][BF$_4$] have clearly shown that only 30% of the PdCl$_2$(PPh$_3$)$_2$ complex (featuring a signal at 28.2 ppm) has been converted to PdCl$_2$(dppp)

(14.0 ppm). Most of the starting complex (70%) has been converted to *cis*-[PdCl(PPh$_3$)$_2$(η^1-dppp)]Cl complex coordinating dppp as a monodentate ligand (δ(P^A) = 27.2 ppm, ^2J(P^A, P^C) = 430 Hz, ^2J(P^A, P^B) = 10 Hz; δ(P^B) = 15.9 ppm, ^2J(P^A, P^B) = 10 Hz, ^2J(P^B, P^C) = 35 Hz; δ(P^C) = 7.4 ppm, ^2J(P^A, P^c) = 430 Hz, ^2J(P^B, P^C) = 35 Hz, δ(P^D) = 0.9 ppm (br s)). P^A, P^B, P^C and P^D denote the two phosphorus of the two PPh$_3$, the coordinated and non-coordinated phosphorus of dppp, respectively. (It has also been proved that the diphosphine might co-ordinate as monodentate ligand in ionic liquids by forming [PtL$_3$Cl]$^+$ type ionic species [31] (L stands for a phosphorus donor of a mono- or bi-dentate phosphine). It has to be added that the formation of complex cations by phosphine–halide ligand exchange reaction is much favoured in ionic liquids than in conventional organic solvents.)

The reaction of PdCl$_2$(PPh$_3$)$_2$ with dppp in [BMIM][PF$_6$] is different from that in [BMIM][BF$_4$]. Complete substitution of PPh$_3$ by dppp took place resulting in PdCl$_2$(dppp) exclusively. The much higher preference of the linear esters **3** in [BMIM][PF$_6$] might be due to the formation of the palladium–diphosphine catalytic intermediates formed from PdCl$_2$(dppp).

5. Conclusions

As a summary, it can be stated that palladium-catalysed hydroalkoxycarbonylation of styrene in butyl-methyl-imidazolium-type ionic liquids can be carried out. Although with moderate yields in most cases, the above systems provide 2- and 3-phenyl-propionates with moderate to high regioselectivities in [BMIM][BF$_4$] and [BMIM][PF$_6$], respectively. The regioselectivity of hydroalkoxycarbonylation is strongly influenced by both the chelating phosphines added and the structure of the alcohol.

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